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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,289	10/01/2003	Kazuhide Inoue	U 014843-4	8299

7590

04/05/2005

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EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 04/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/676,289	Applicant(s) INOUE ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-41 is/are pending in the application.
- 4a) Of the above claim(s) 10-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/28/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's affirmation of the species election of Ca²⁺ in the reply filed December 28, 2004 is acknowledged.

Claim Rejections - 35 USC § 102

The rejection of record of claims 1 and 3-9 under 35 USC 102(b) is withdrawn in view of the claim amendments submitted December 28, 2004.

Claims 1 and 3-9 are maintained as rejected under 35 U.S.C. 102(a) as being anticipated by Tsuda et al. (P2X4 receptors induced in spinal microglia gate tactile allodynia after nerve injury, *Nature*, 14 August 2003, vol 424 p778-783 and supplemental information).

The three disclaiming affidavits or declarations filed under 37 CFR 1.132 filed December 28, 2004 are insufficient to overcome the rejection of claims 1-9 based upon 35 USC 102(a) as set forth in the last Office action because: the declarations do not fulfill the requirements for declarations under 37 CFR 1.132 as described in MPEP 715.04 (II) and 37 CFR 1.68. Specifically, the declarations do not contain the required statements regarding 18 USC 1001 and that all statements made by declarant are true.

Claim Rejections - 35 USC § 103

Claims 1 and 3-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al. (Pharmacological Characterisation of the Human P2X₄ Receptor Using the FLIPR, *Pharmacology Reviews and Communications*, vol. 10, p341-347) in view of Tsuda et al. (Mechanical Allodynia Caused by Intraplantar Injection of P2X Receptor Agonist in Rats: Involvement of Heteromeric P2X_{2/3} Receptor Signaling in Capsaicin-Insensitive Primary Afferent Neurons, *Journal of Neuroscience*, 2000, vol 20, p RC90/1-RC90/5).

1. Wood et al. teach the characterization of human P2X₄ receptor. The receptor is expressed in human astrocytoma cell line 132 1N1, a mammalian cell line. The response of the P2X₄ receptor is measured by determining the Ca²⁺ ion flux in the presence of agonist and/or antagonist. Measurements were done with the antagonist incubated with the cell before addition of the agonist. Measurements were also done without antagonist (ie, as described in Materials and methods, with buffer alone). Wood et al. teach that ATP has no effect on non-transfected cells, indicating that the cloned P2X₄ receptor is the only P2X receptor present. Thus Wood et al. teach steps (a) and (b) of the method of claim 1 and the limitations of claims 3-9. Wood et al. do not teach that this method can be used to identify compounds useful in the treatment of neuropathic pain.

2. Tsuda et al. teach that injection of P2X receptor agonists into rats caused mechanical allodynia and that this allodynia could be reversed by pre-treatment with P2X receptor antagonists. Tsuda et al. hypothesized the type of P2X receptor responsible for the results they reported, but were unable to exclude the possibility that

other receptors were involved. They state: "...the discovery of new selective antagonists...for each P2X receptor subtype is awaited to clarify our hypothesis". (see page 4) Later in their conclusion (pages 4-5), Tsuda et al. state that P2X receptors are believed to play a role in pain and further state that "...the mechanisms underlying P2X receptor-mediated mechanical allodynia may be one of the determining factors of the mechanical allodynia in these painful states. Elucidation of this pathway may lead to the discovery of a new class of compounds that suppress mechanical allodynia in pathological pain."

3. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the method of Wood et al. to identify compounds useful in the treatment of neuropathic pain as taught by Wood et al. Tsuda et al. provided a motivation to do so, teaching a relationship between P2X receptors and pain and stating the desirability of new compounds for the suppression of pain. A person of ordinary skill in the art would have had a reasonable expectation of success in using the method taught by Wood et al. to identify compounds useful in the treatment of neuropathic pain because Wood et al. taught their method to identify antagonists of P2X₄ receptors using techniques well known in the art and demonstrate this method actually successfully identifies P2X₄ receptor antagonists. Therefore, the invention of claims 1 and 3-9 would have been obvious, as a whole, at the time the instant invention was made.

Response to Arguments

4. Applicant's arguments filed December 28, 2004 have been fully considered but they are not persuasive. Applicant states that because there are 7 subtypes of P2X receptors which can form hetero-oligomers and because there are numerous types of

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pain, the person of ordinary skill in the art would not have a reasonable expectation of success in selecting a combination of P2X4 receptor and tactile allodynia from the teachings of Tsuda et al. This argument is not persuasive as the expectation of success in the obviousness rejection does not refer to the specific combination of receptor and type of pain, but instead refers to whether the person of ordinary skill would expect success in combining the teachings of Wood et al. and Tsuda et al. to perform the steps of the claimed method. The claimed method has been amended to change the intended use of the method, but the individual steps themselves are no different than originally filed.

5. Applicant further states that the mechanical allodynia researched by Tsuda et al. is essentially different from the tactile allodynia disclosed in the instant application because the mechanical allodynia described by Tsuda et al. is acute and temporary while the tactile allodynia disclosed by applicant is caused by nerve damage and is a chronic condition. This is not found persuasive because although the causes of the pain described by applicant and taught by the reference of Tsuda et al. are different the result is the same: both conditions are allodynia. Further, applicant uses both terms in the specification, indicating there is similarity between the two conditions. On page 20 lines 19-20 the result of nerve injury in rats is referred to as mechanical allodynia.

6. Applicant further asserts that since the P2X4 receptor has been associated with disorders other than pain it can not be directly associated with pain. This is not found persuasive as the teachings of Tsuda et al. refer generally to P2X receptors with regard to pain and do not exclude any particular subtype. Since there are general teachings

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associating P2X receptors with pain it is not unreasonable to *prima facie* associate the specific P2X4 subtype with pain.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

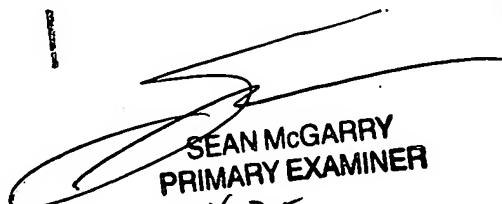
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contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
March 24, 2005


SEAN McGARRY
PRIMARY EXAMINER
1635